

# *Ventricular arrhythmias due to LV dysfunction or LV dysfunction due to frequent VAs – the hen or the egg?*

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# Agenda

- Definition
- Pathophysiology
- Clinical factors for development of LV dysfunction
- Risk stratification
- Drugs vs ablation



# Arrhythmia induced cardiomyopathy

## Definitions

- AICM is a condition, in which atrial or ventricular tachyarrhythmias or frequent PVCs result in reversible LV dysfunction and systolic HF
  - PVC-induced CMP (*arrhythmia induced*)
  - PVCs-worsened CMP (*arrhythmia mediated*)
- CMP with superimposed PVCs

# PVCs vs primary cardiomyopathy

**The old chicken – egg dilemma..**



EDITORIALS

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## Tachycardia and Cardiomyopathy: The Chicken-Egg Dilemma Revisited\*

JOHN J. GALLAGHER, MD, FACC

*Charlotte, North Carolina*

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The effect of an *acute* increase in heart rate on left ventricular function has been well documented in patients with paroxysmal arrhythmias. There is general agreement that cardiac output remains relatively constant despite a decrease in stroke volume and end-diastolic volume. These changes may be accompanied by minor wall motion abnormalities. Nonetheless, in the absence of other heart disease, initiation of supraventricular tachycardia has not resulted acutely in any overall decrease in ejection fraction compared with baseline function in sinus rhythm (1). Similarly, no appreciable change in ejection fraction has been observed in normal subjects despite atrial pacing to rates of 120 to 160 beats/min (2-4).

identify "improvement" is somewhat limited, since the initial measure of left ventricular function may have been artificially low because of a rapid heart rate. Nonetheless, the continued late improvement noted supports the concept that chronic tachycardia may have resulted in a reversible form of cardiomyopathy.

**Chronic tachycardia and left ventricular dysfunction.** Chronic supraventricular tachycardia was once regarded as a benign process without adverse myocardial sequelae (6,7). Subsequently, however, a relation between incessant tachycardia and cardiomyopathy has been suggested by a number of investigators (8-14). Data from my laboratory support this concept (15). Nine patients (aged 5

# PVCs as the reversible cause of cardiomyopathy

Original Article



## Suppression of Frequent Premature Ventricular Contractions and Improvement of Left Ventricular Function in Patients With Presumed Idiopathic Dilated Cardiomyopathy

DOUGLAS F. DUFFEE, M.D.,\* WIN-KUANG SHEN, M.D., AND HUGH C. SMITH, M.D.

- 14 pts with ectopy >20,000/24 hours and impaired LV EF
- Suppression of ectopy (>75%) using amiodarone in 5 pts
- Improvement of LV EF from  $27 \pm 10\%$  to  $49 \pm 17\%$  ( $p < 0.05$ )
- **Conclusions: ectopy may be the cause of reversible CMP**



# Or by ablation...

## First Evidence of Premature Ventricular Complex-Induced Cardiomyopathy: A Potentially Reversible Cause of Heart Failure

SUMEET S. CHUGH, M.D., WIN-K. SHEN, M.D., DAVID M. LURIA, M.D.,  
and HUGH C. SMITH, M.D.

From the Cardiovascular Division, Department of Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

**PVC-Induced Cardiomyopathy.** Tachycardia-induced cardiomyopathy is a well-recognized and reversible condition, but left ventricular dysfunction due to frequent isolated premature ventricular complexes (PVCs) has not been reported. We observed resolution of dilated cardiomyopathy in a patient after a focal source of PVCs was eliminated by radiofrequency ablation. In a subset of patients with heart failure, PVC-induced cardiomyopathy may be a potentially reversible cause of left ventricular dysfunction. (*J Cardiovasc Electrophysiol*, Vol. 11, pp. 328-329, March 2000)

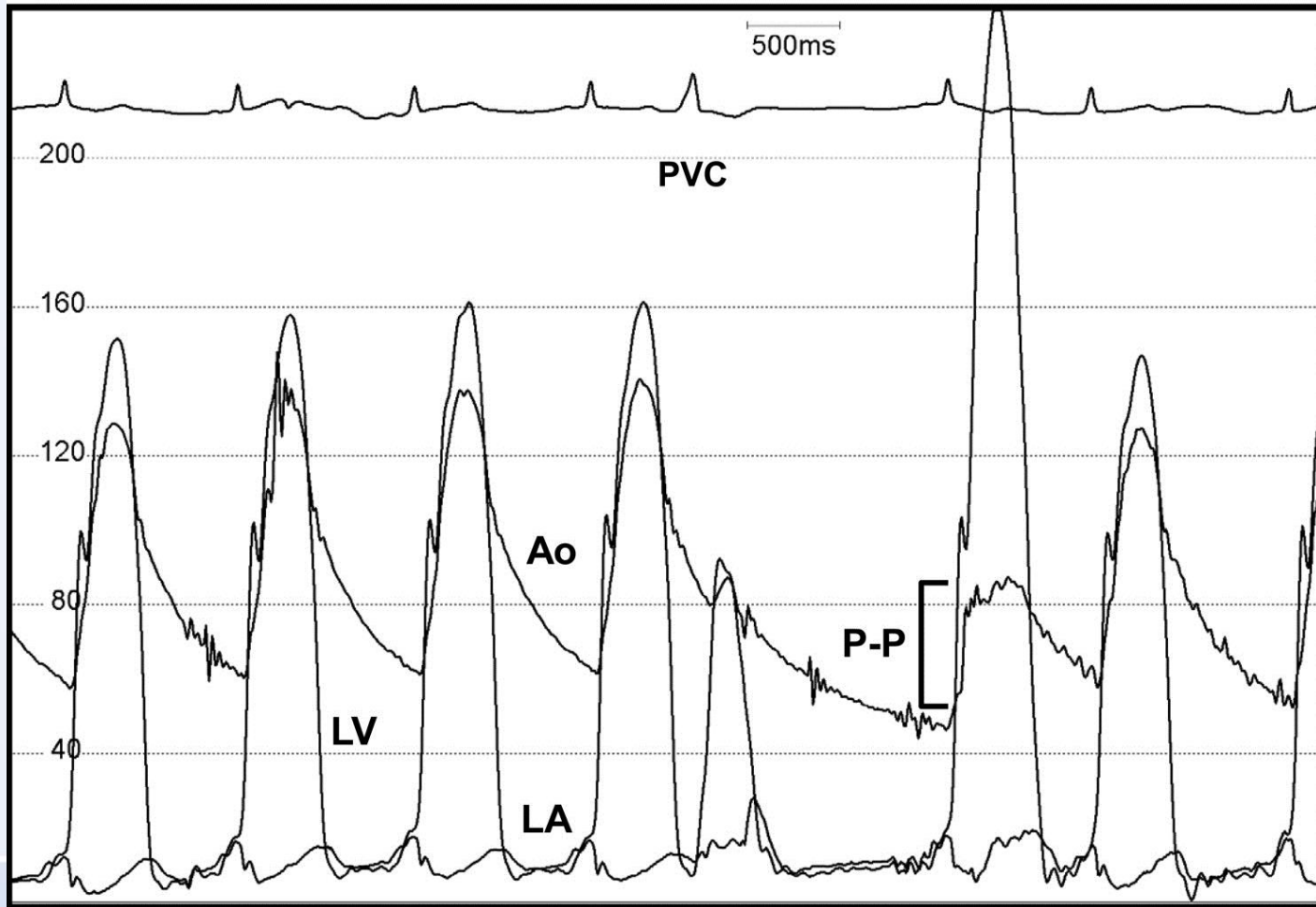
# Pathophysiology

## PVC induced/worsened cardiomyopathy

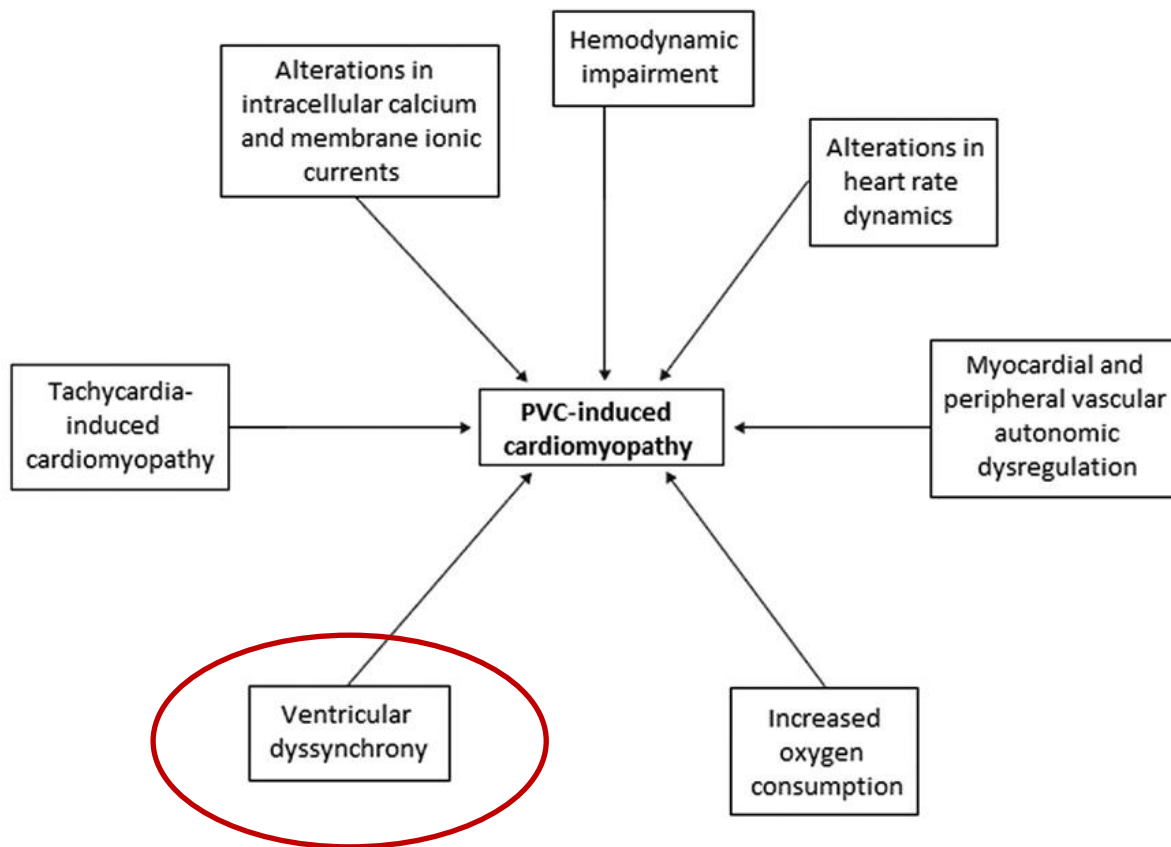




# Pulse deficit during PVCs



# Pathophysiology of AICM



Gopinathannair, R. et al. J Am Coll Cardiol. 2015; 66(15):1714-28.

In animal models of PVC induced CMP no evidence of inflammation, apoptosis, fibrosis.

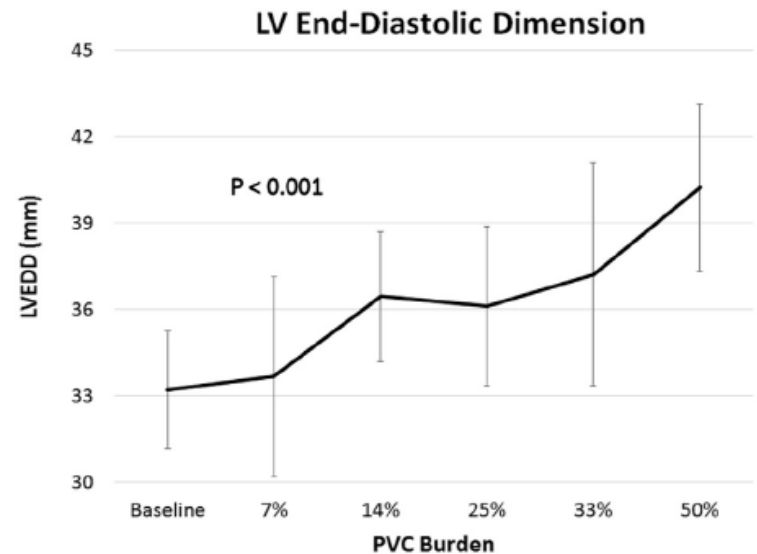
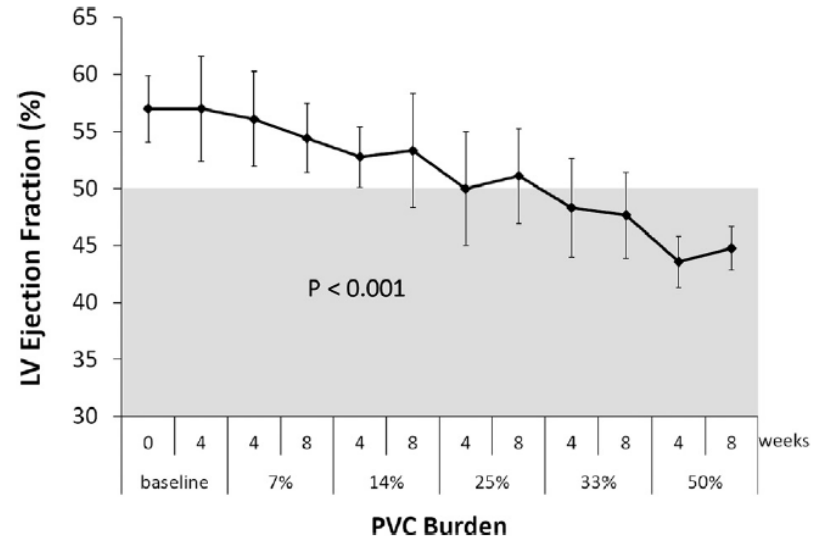
Dyssynchrony during PVC hypothesized as potential mechanism, but CMP may be induced also by PACs

Cha et al Circ EP 2012;5:229-236  
Huizar et al Circ EP 2011;4:543-9.  
Hasdemir et al Europace 2013;15:1790

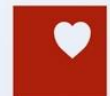
# Pathophysiology

## Animal data

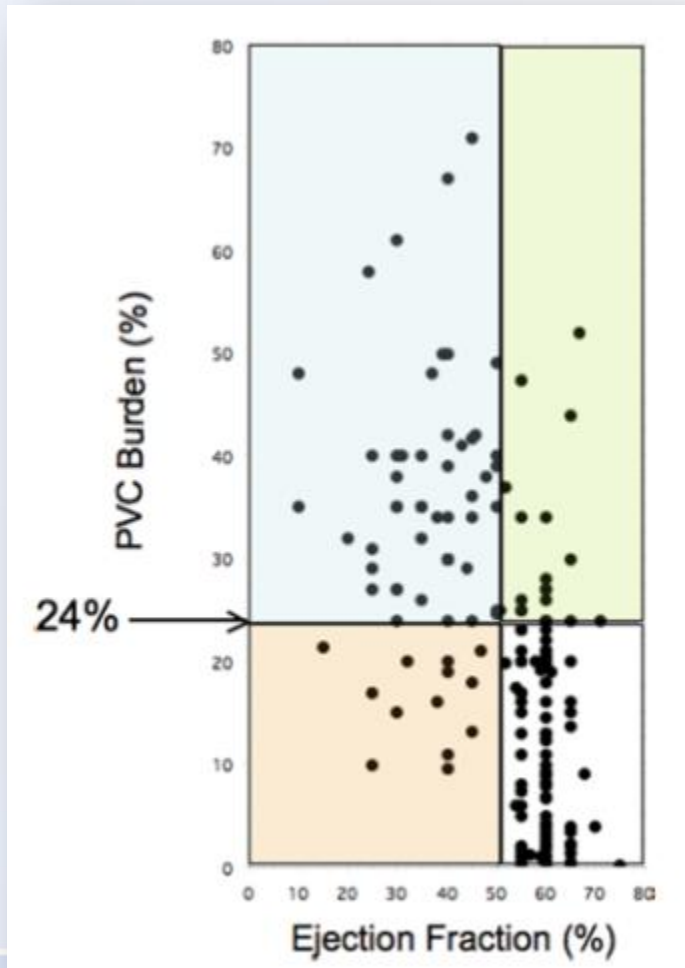
- 9 mongrel dogs
- RV apical PVCs (240ms CI)
- Burden 0%, 7%, 14%, 25%, 33%, 50% for 8weeks
- PVC induced CMP in some canines with 25%, 33% but all with 50%
- No changes in BNP and interleukin 6 levels.
- **LV systolic function declined linearly as PVC burden increased**



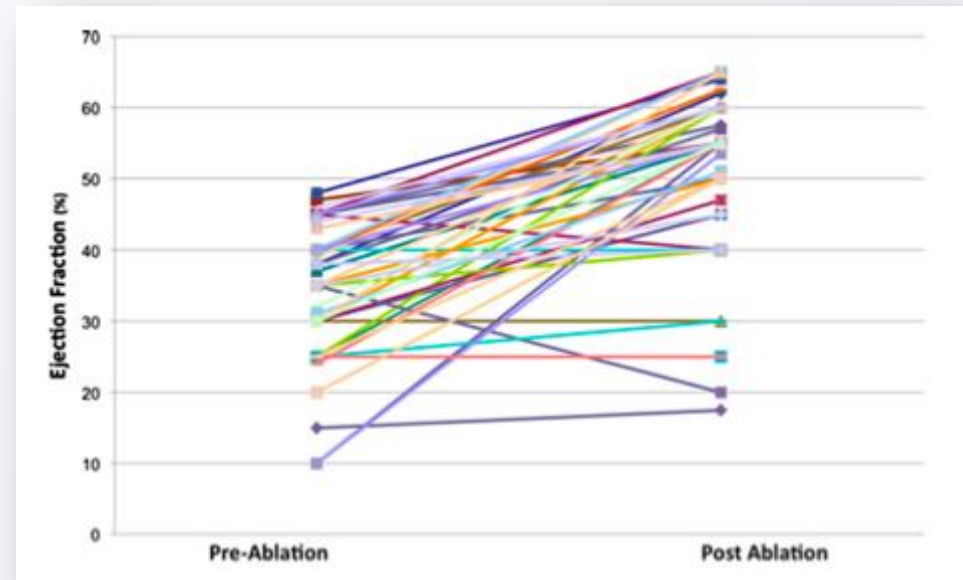
# Which clinical factors are associated with PVC induced CMP?



# What level of PVCs is critical?



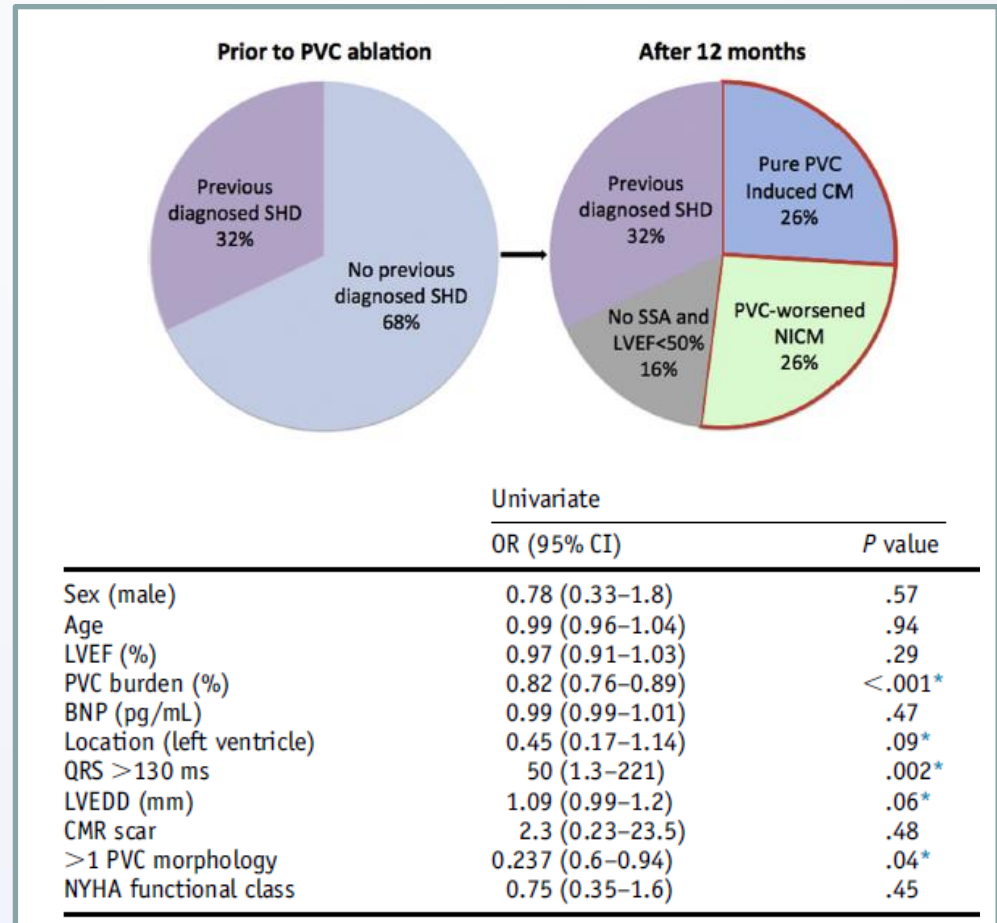
- 174 pts with PVCs (24-hour Holter)
- LVEF (mean.  $0.37 \pm 0.10$ ) in 57 (33%)
- Ablation led to improvement of LVEF





# Which factors are associated with normalization of EF after ablation?

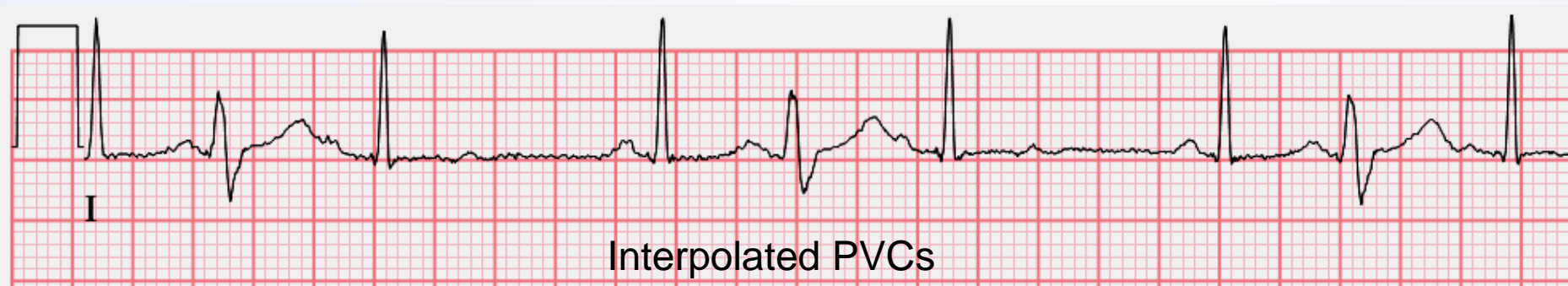
- Prospective multicenter trial
- 155pts with LV dysfunction and frequent PVCs without known SHD
- 49% had normalization of LVEF
- Factors associated with pure PVC induced CMP:
  - Baseline PVC burden >17%
  - Intrinsic QRS <130ms
  - EDDL <63mm



Penela et al. Heart Rhythm 2017;14:1864-1870.

# Other factors influencing significance of VAs

## Timing, location, symptoms and ...



Interpolated PVBs lead more often to CMP

\*Asymptomatic course, epicardial location of PVCs, **retrograde P wave**

Sun et al. *Int J Cardiovascular Imaging* 2003;19:925

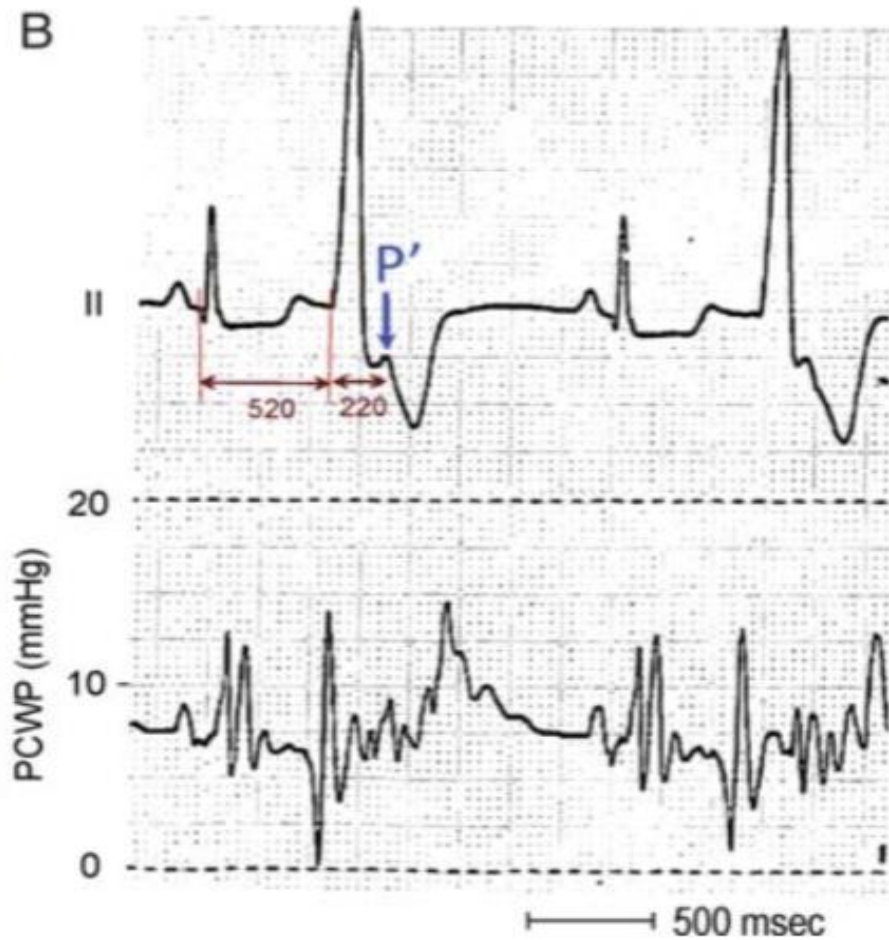
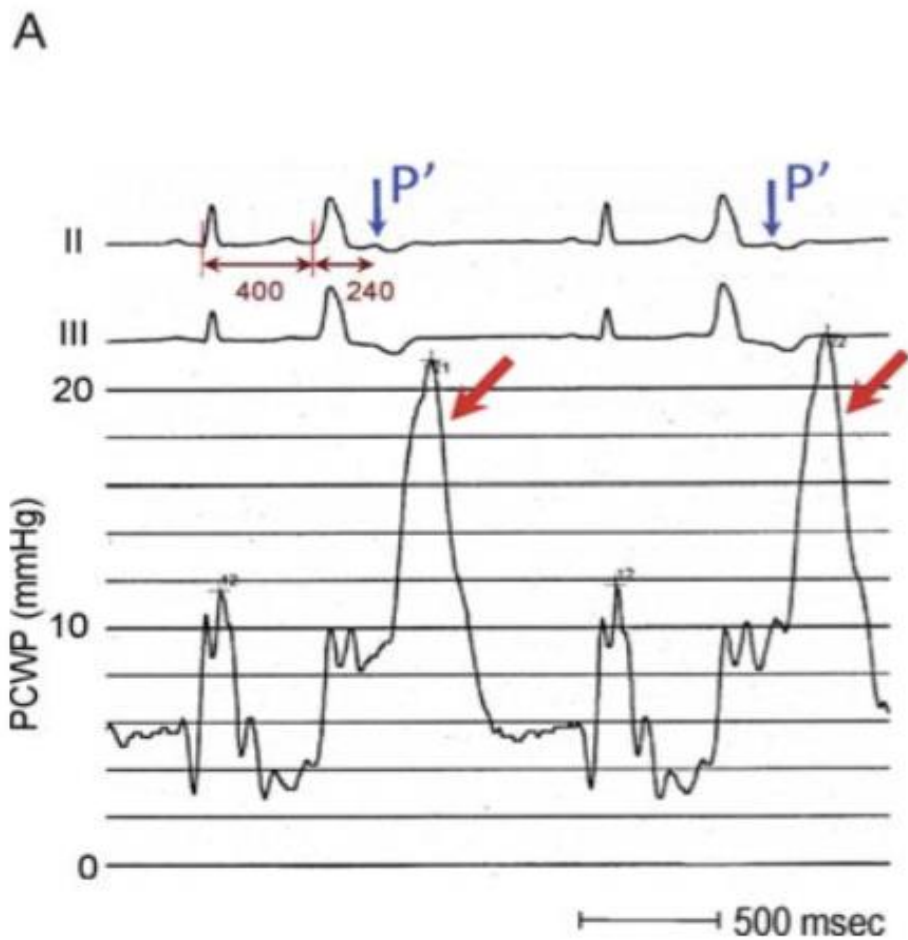
\*Ban JE, *Europace* 2013;15:735-741.

\*Blaye-Felice MS, *Heart Rhythm* 2016;13:103-110.

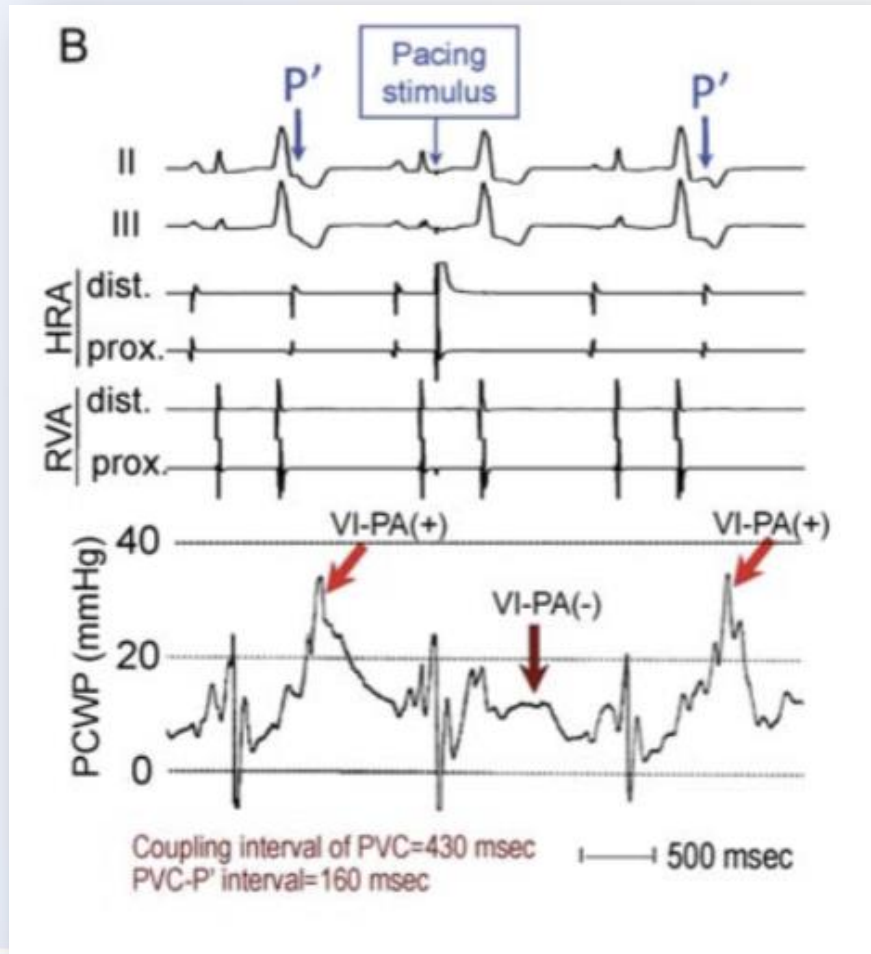
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# Augmentation of PCWP after PVC



# Improvement after ablation was higher in pts with augmentation



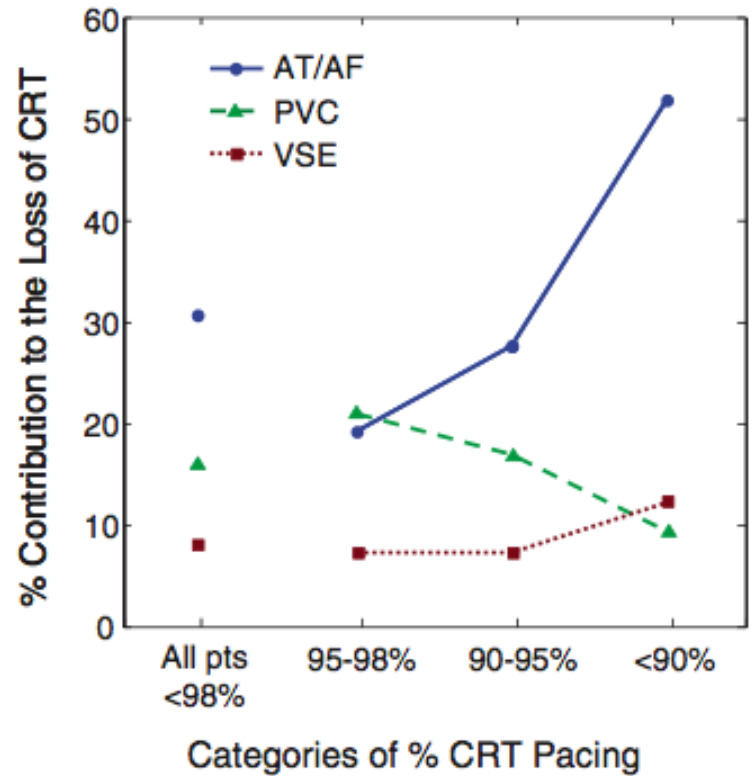
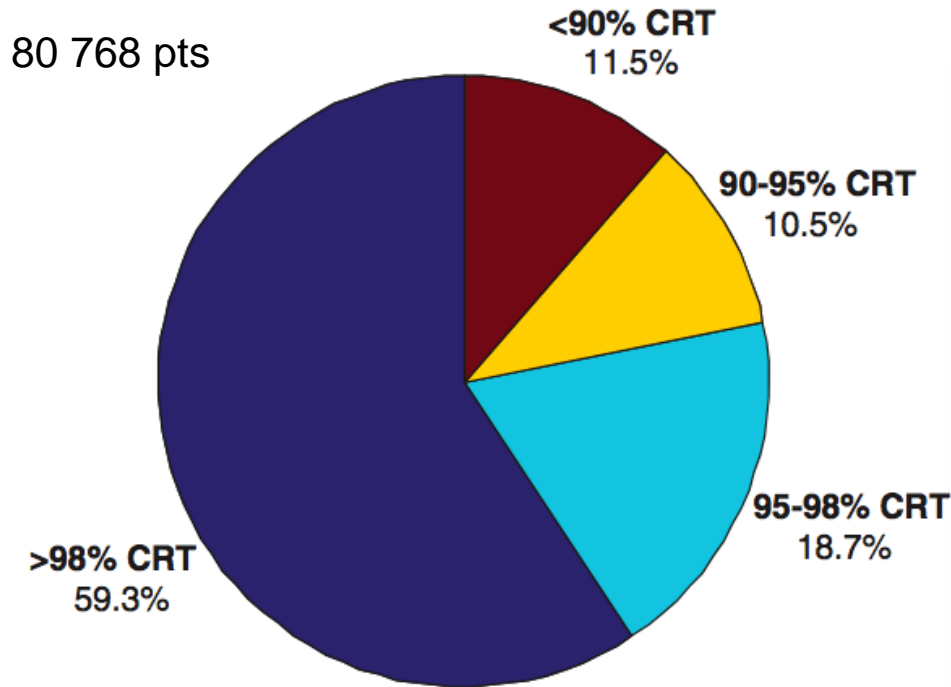
- 7.4 + 0.9 months
- Echo parameters and BNP improved in group with augmentation
- PVC coupling interval < 500 ms and presence of retrograde P wave (PVC-P' interval < 300ms) predicted augmentation with high sensitivity

# Frequent PVCs and CRT



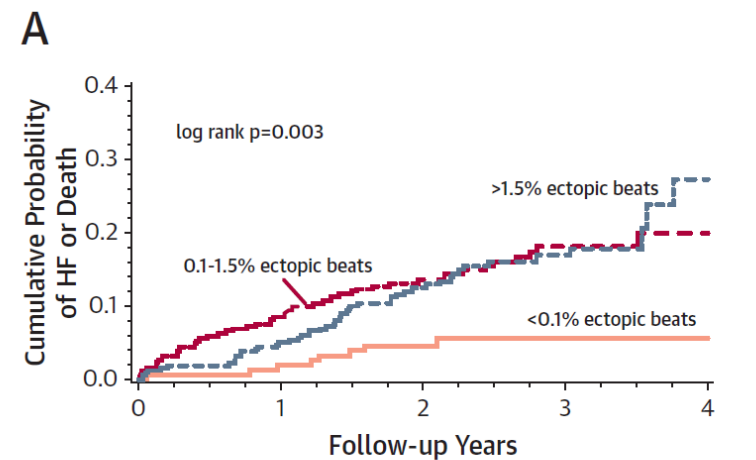


# PVCs as reason for loss of BiV capture



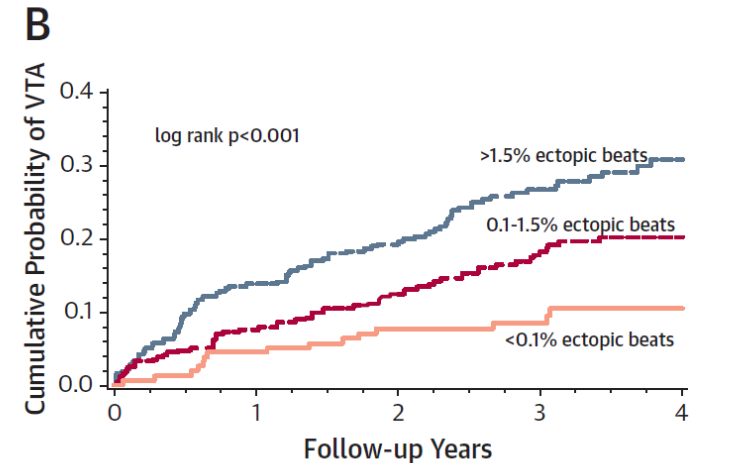
# What is significance of PVCs in CRT recipients?

- Analysis of MADIT CRT study
- Prior implantation  $3.2 \pm 5.5\%$  PVCs/24 hour monitoring
- Patients with  $>0.1\%$  ectopy beats less chance of reverse remodeling and higher risk of HF/death/VA



Patients at Risk

160	156 (0.02)	106 (0.05)	41 (0.05)	12 (0.05)
321	291 (0.08)	202 (0.14)	93 (0.18)	24 (0.20)
320	302 (0.05)	192 (0.12)	93 (0.17)	16 (0.27)

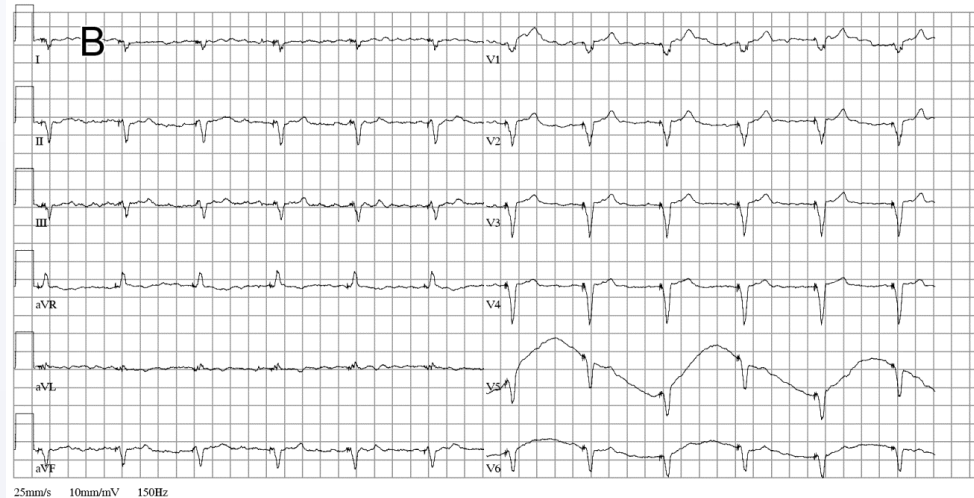
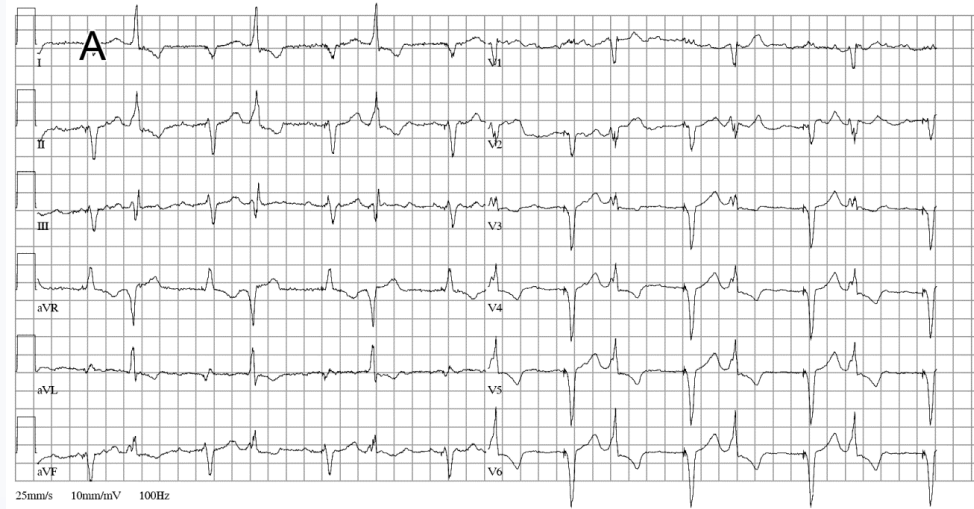


Patients at Risk

160	151 (0.04)	140 (0.08)	96 (0.08)	35 (0.10)
321	288 (0.08)	262 (0.12)	178 (0.18)	80 (0.20)
320	273 (0.14)	240 (0.19)	147 (0.27)	60 (0.31)

# Frequent PVCs vs CRT

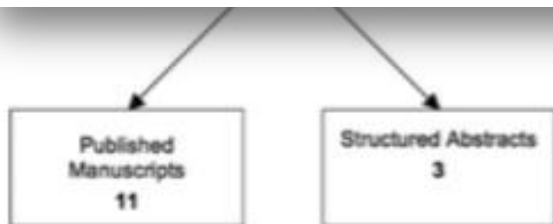
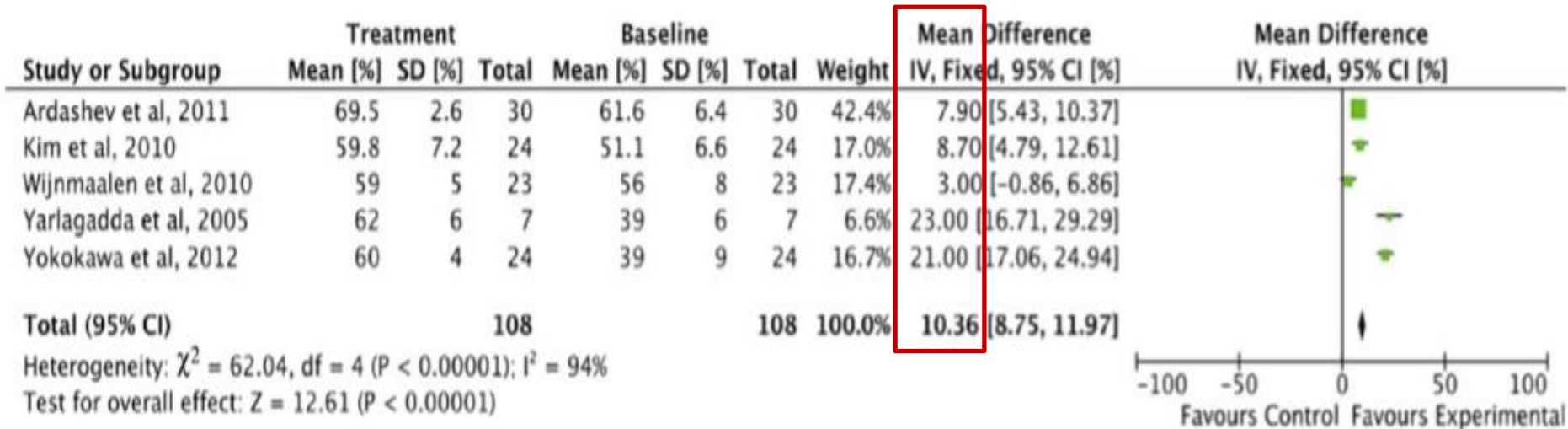
- 65 pts with CRT
- Nonresponders >10,000 PVCs/24hours
- RF ablation of 76 foci
- Improvement after ablation:
  - LV EF -  $26\pm 5\%$  to  $33\pm 7\%$  ( $p<0.001$ )
  - LV volume -  $178\pm 72$  to  $145\pm 32$ ml
  - NYHA - III to II ( $p<0.001$ )
- **In multivariate analysis improvement of EF in pts with frequent ectopy more than 22%/24 hours**



# Does elimination of PVCs lead to clinically relevant improvement?



# Catheter ablation of ectopy improves LV EF

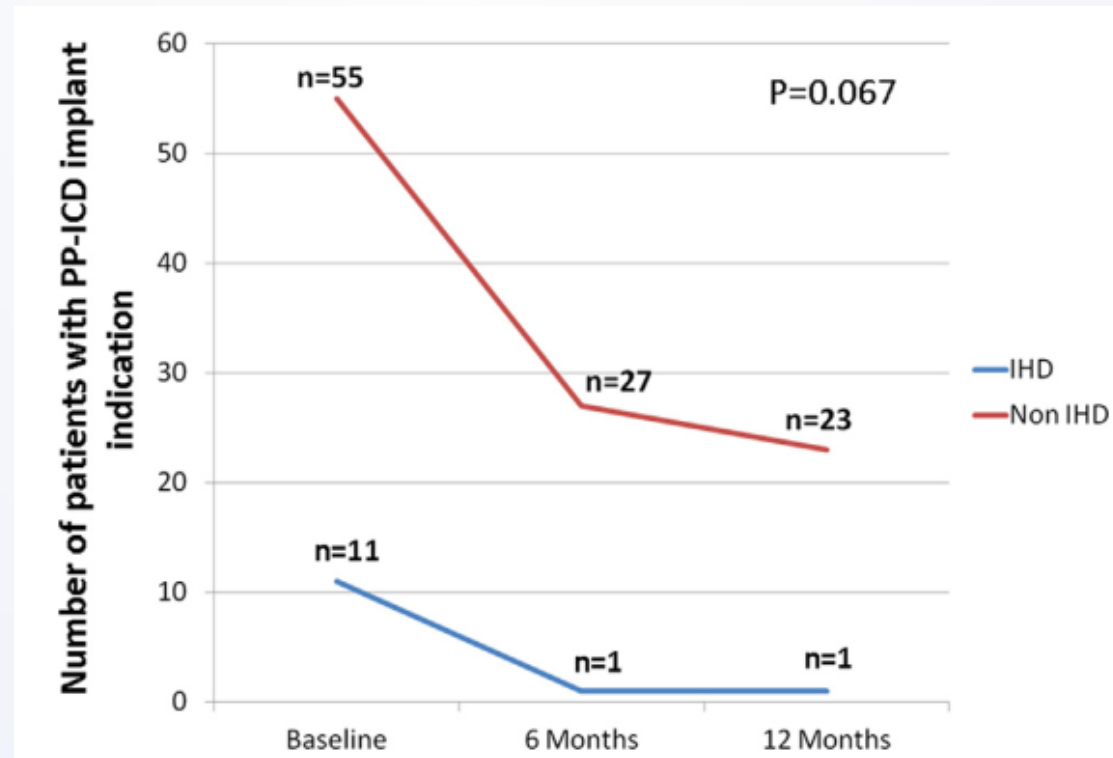


Lamba J, et al. PACE 2014, 37: 73-8



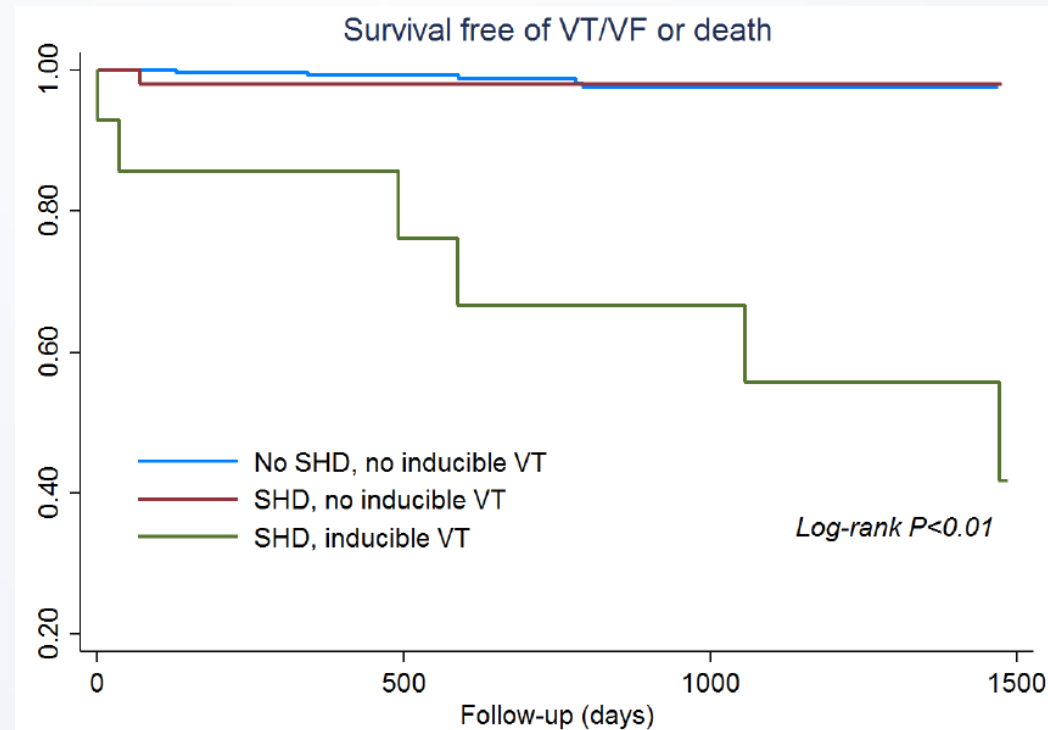
# In pts with LV dysfunction may prevent prophylactic implantation of ICD....

- 66pts with frequent PVCs, EF LV <35% suitable for primary prophylactic ICD implantation
- After ablation
  - EF LV improved from  $28\pm 4\%$  to  $42\pm 12\%$
  - 42pts (64%) not fulfilled the indication criteria for ICD implant



# Risk stratification of patients with frequent PVCs

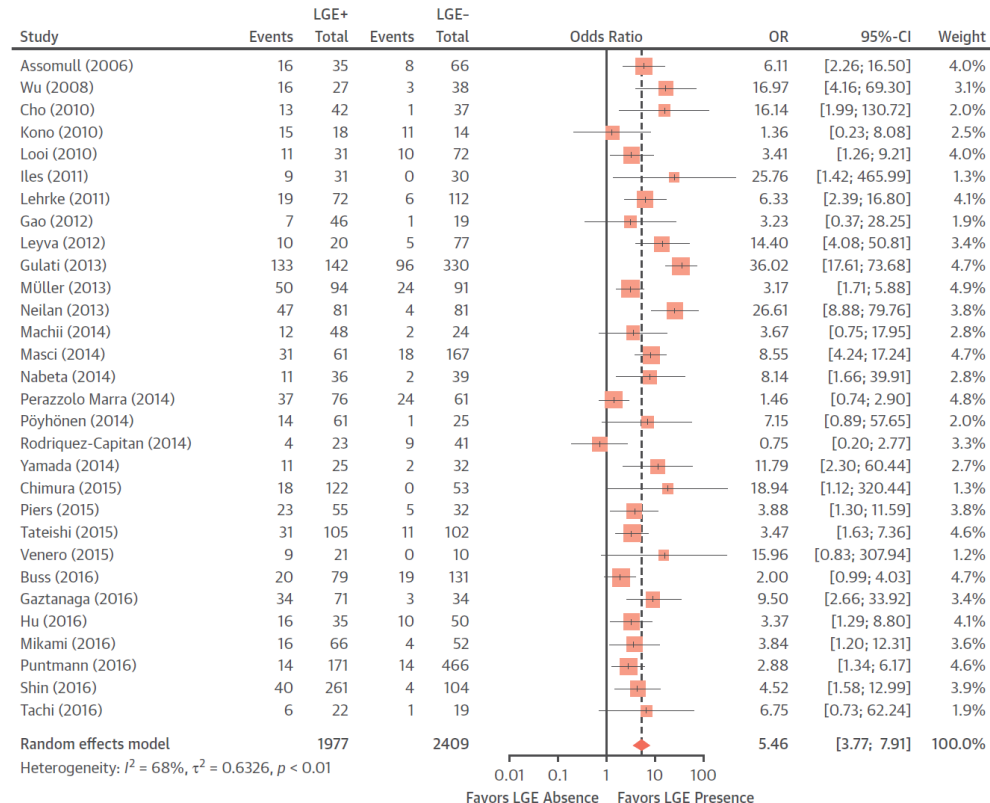
- 321 pts undergoing PVC ablation
- SHD detected in 20% by MRI prior ablation
- VT inducible by PES performer during ablation in 5% of pts
- Highest event rate in pts with LGE and positive PES despite „preserved“ EF



# Risk stratification of patients with NICM

- Metanalysis of LGE significance on MRI in pts with NICM
- 34 studies – 4.554pts
- LGE present in 45%pts
  - Mortality
    - Odds ratio 3.4 (95% CI 2.0-5.7)
  - Ventricular arrhythmias
    - Odds ratio 4.5 (95% CI 3.4-6.0)
  - Rehospitalization for HF
    - Odds ratio 2.7 (95% CI 1.7-4.2)

FIGURE 2 Combined Endpoint of Any Major Adverse Cardiovascular Events



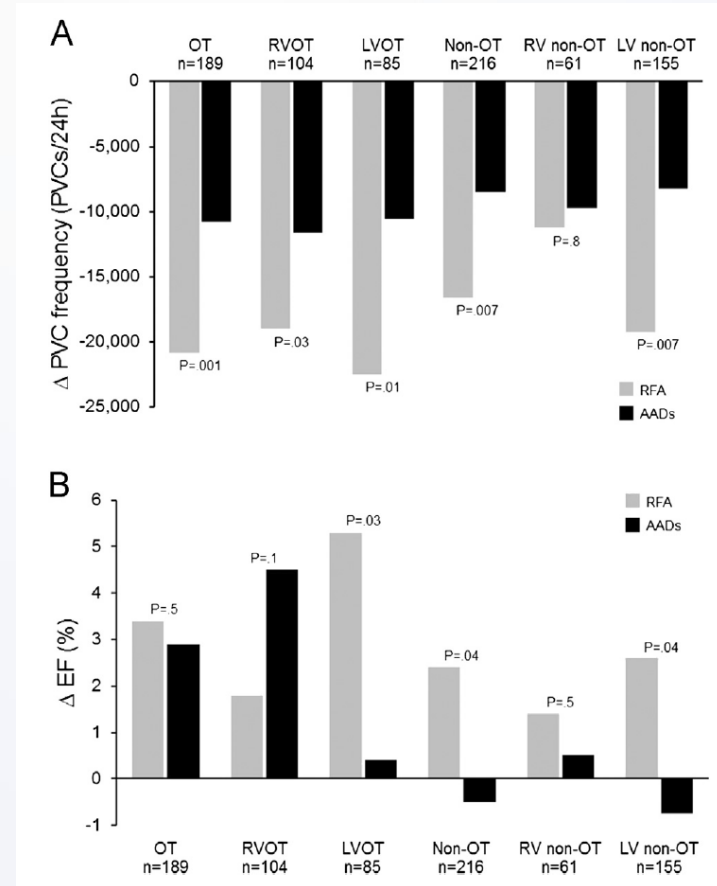
# How to suppress PVCs?



# Drugs vs ablation

## Which is better?

- Retrospective analysis
- 510pts with >10k PVCs treated either by ablation (215pts) or AA drugs (295pts)
- LVEF increased significantly after ablation but not drugs
- Of 121pts with reduced function baseline, LVEF normalized in 47% in ablation, but only in 21% in drug group



# Drugs vs ablation...

- **Pharmacologic treatment:**
  - BB, amiodarone???
- **When to ablate?**
  - Monomorphic (bimorphic) morphology

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref. <sup>c</sup>
In patients with frequent symptomatic PVC or NSVT:			
– Amiodarone should be considered.	<b>IIa</b>	<b>B</b>	64
– Catheter ablation should be considered.	<b>IIa</b>	<b>B</b>	341–343
Catheter ablation should be considered in patients with LV dysfunction associated with PVCs.	<b>IIa</b>	<b>B</b>	341–343

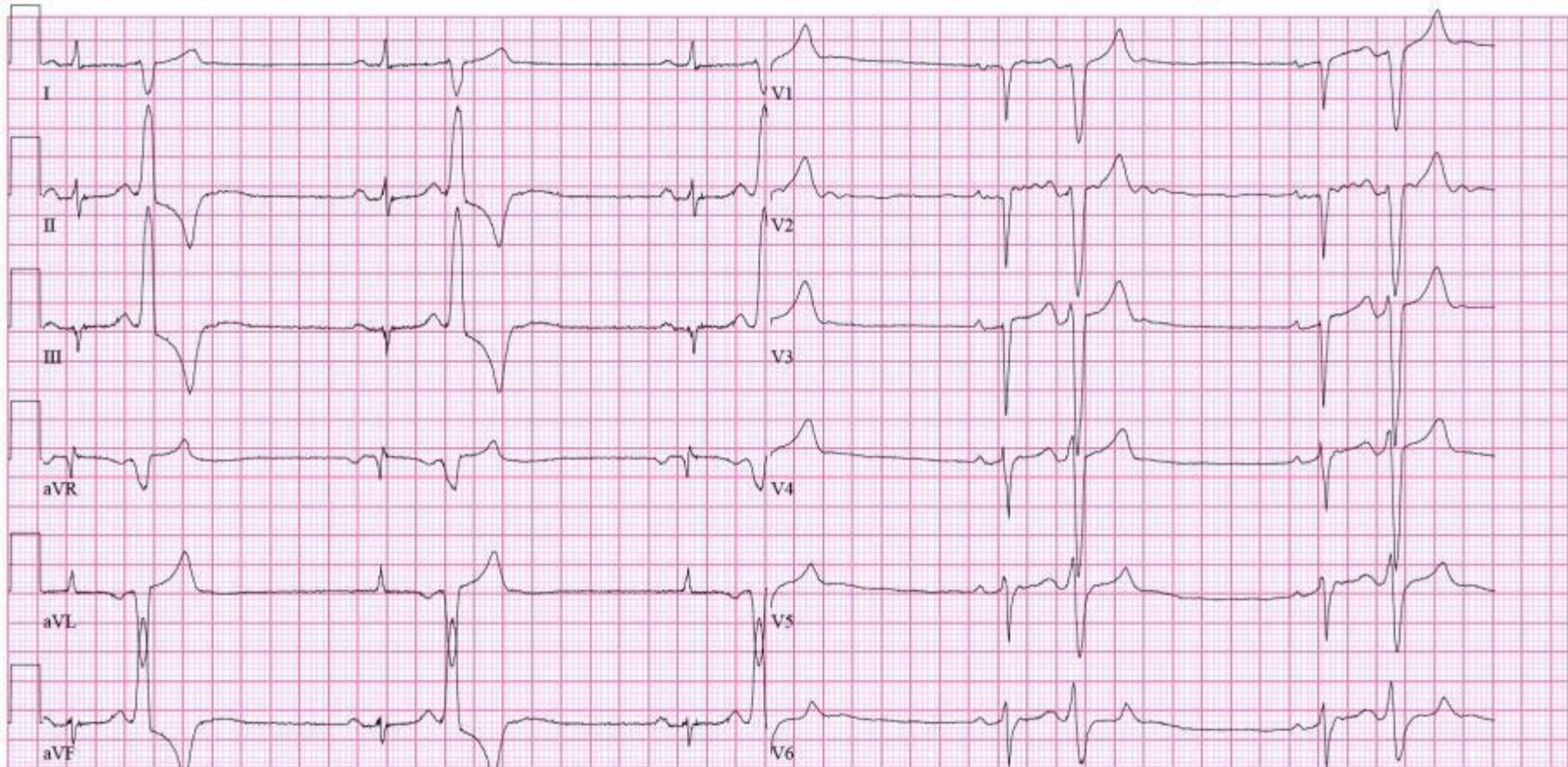
Priori S, et al.  
2015 ESC Guidelines.  
EHJ 36 (2015) 2793–2867

	Symptoms -	Symptoms +
Impaired EF -	Watchful waiting	<b>Treatment</b>
Impaired EF +	<b>Treatment</b>	<b>Treatment</b>



# PVCs from anteroseptal RVOT

## “Easy” target for ablation

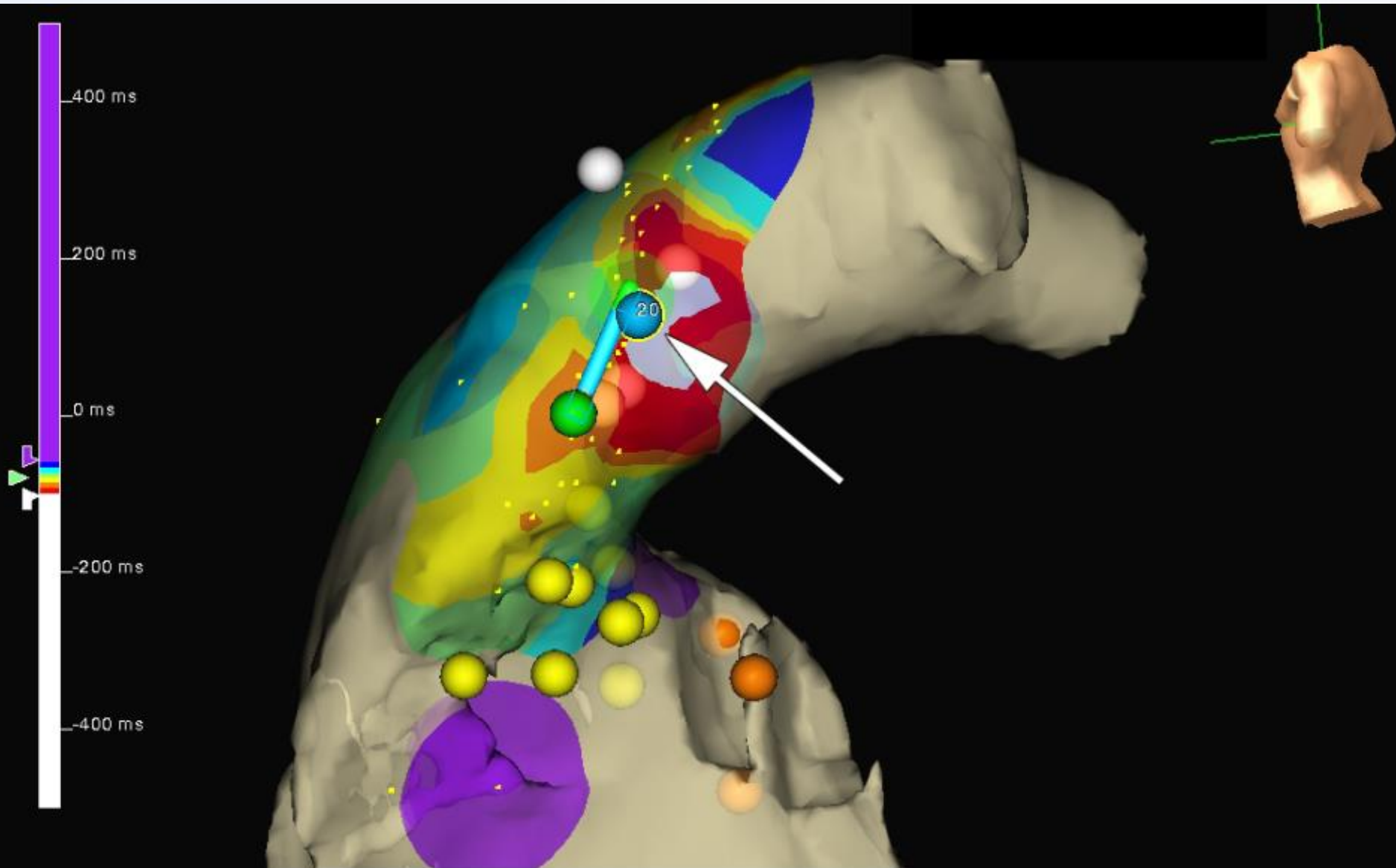


### SUMMARY

- 99421 QRS complexes
- 23796 Ventricular ectopics which represent 23 % of total QRS complexes
  - 0 Supraventricular ectopics which represent <1 % of total QRS complexes
  - 0 Paced QRS complexes which represent <1 % of total QRS complexes

# PVCs from anteroseptal RVOT

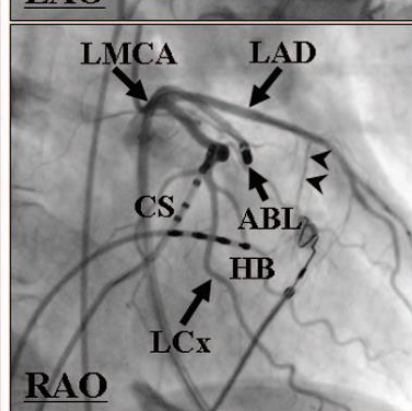
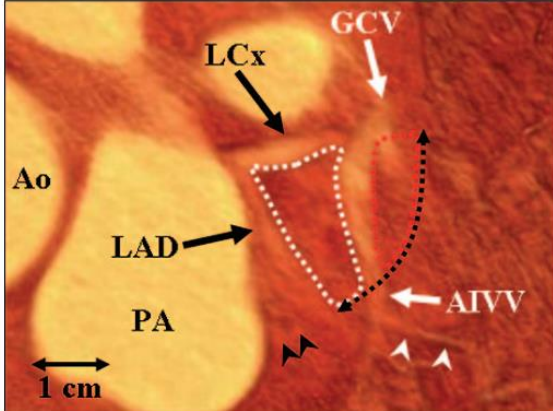
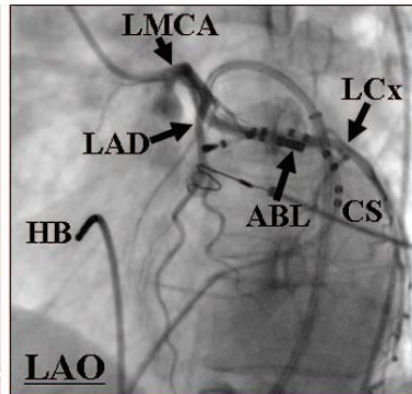
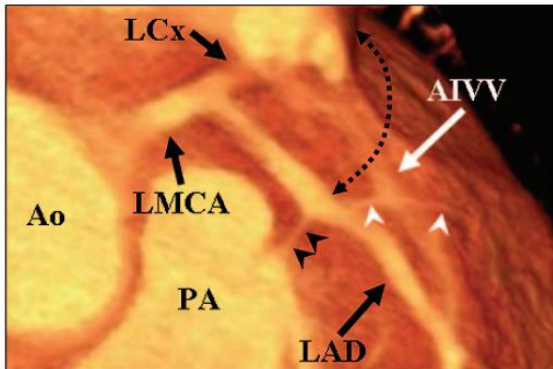
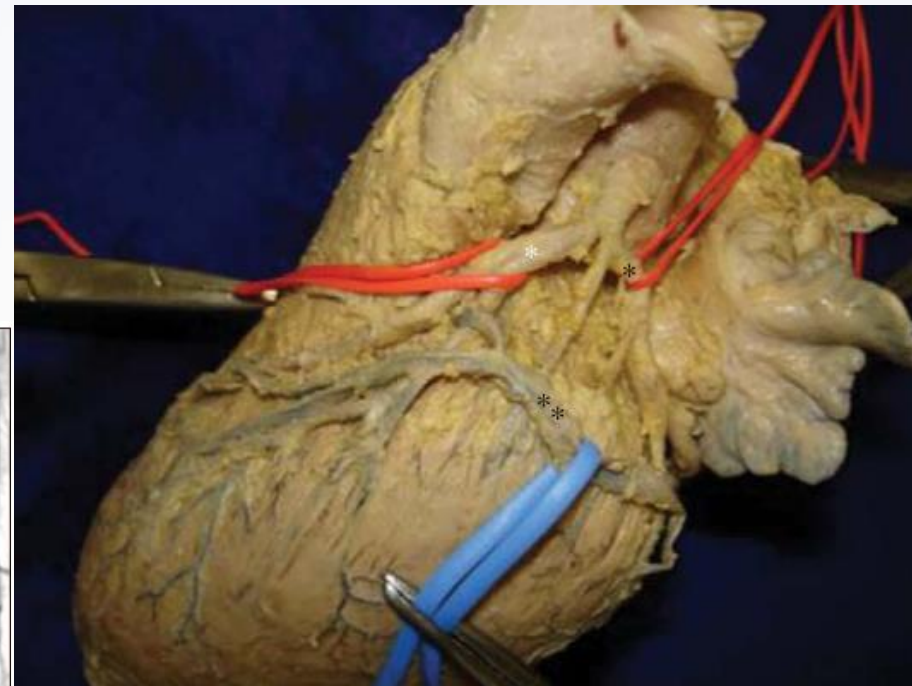
“Easy” target for ablation





# PVCs from LV summit

Not that easy target

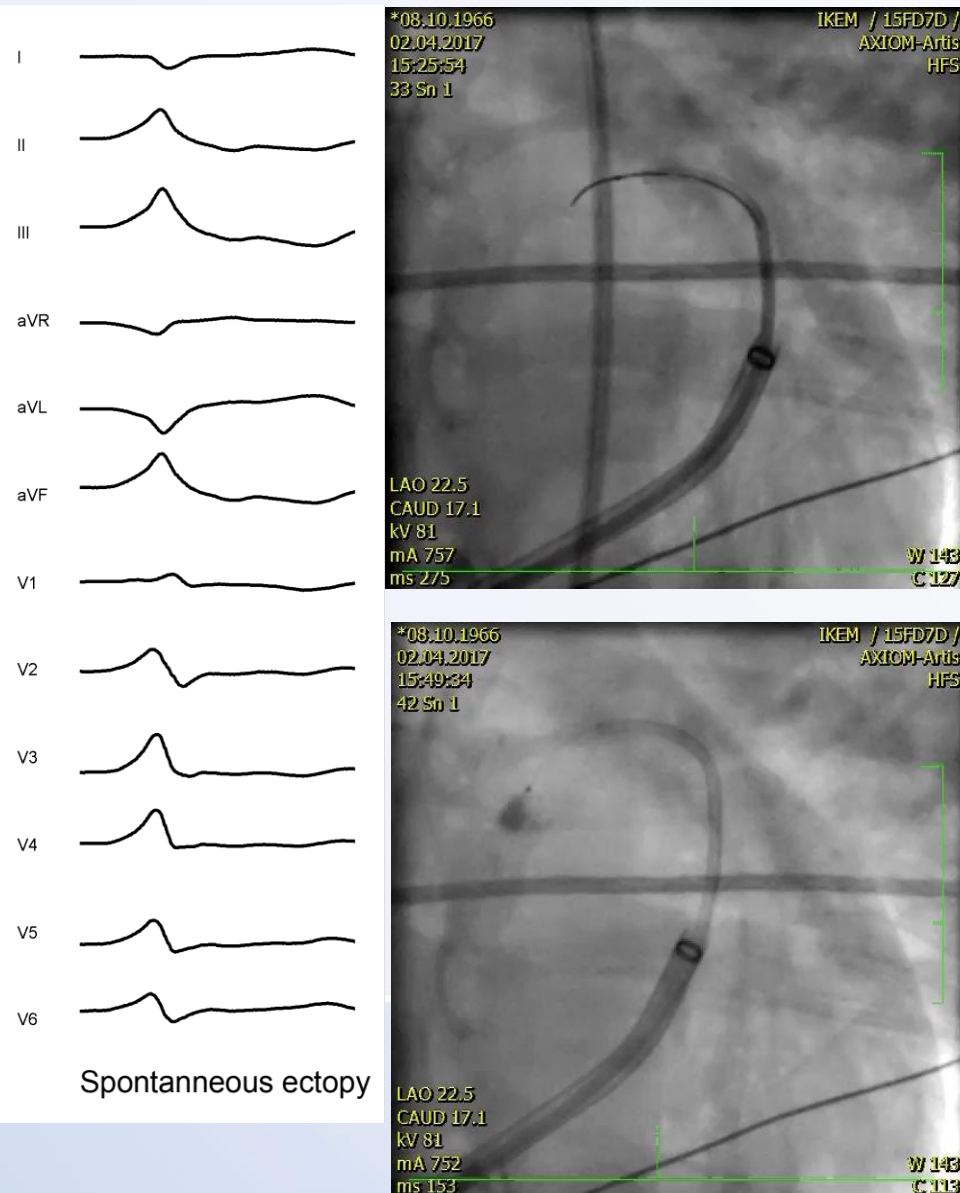


- Def.: area between bifurcation of LAD and LCx
- GCV divides this into two parts:
  - Superior inaccessible part
  - Inferior part accessible by percutaneous epicardial ablation

T Yamada *Circ EP* 2010;3:616-623.

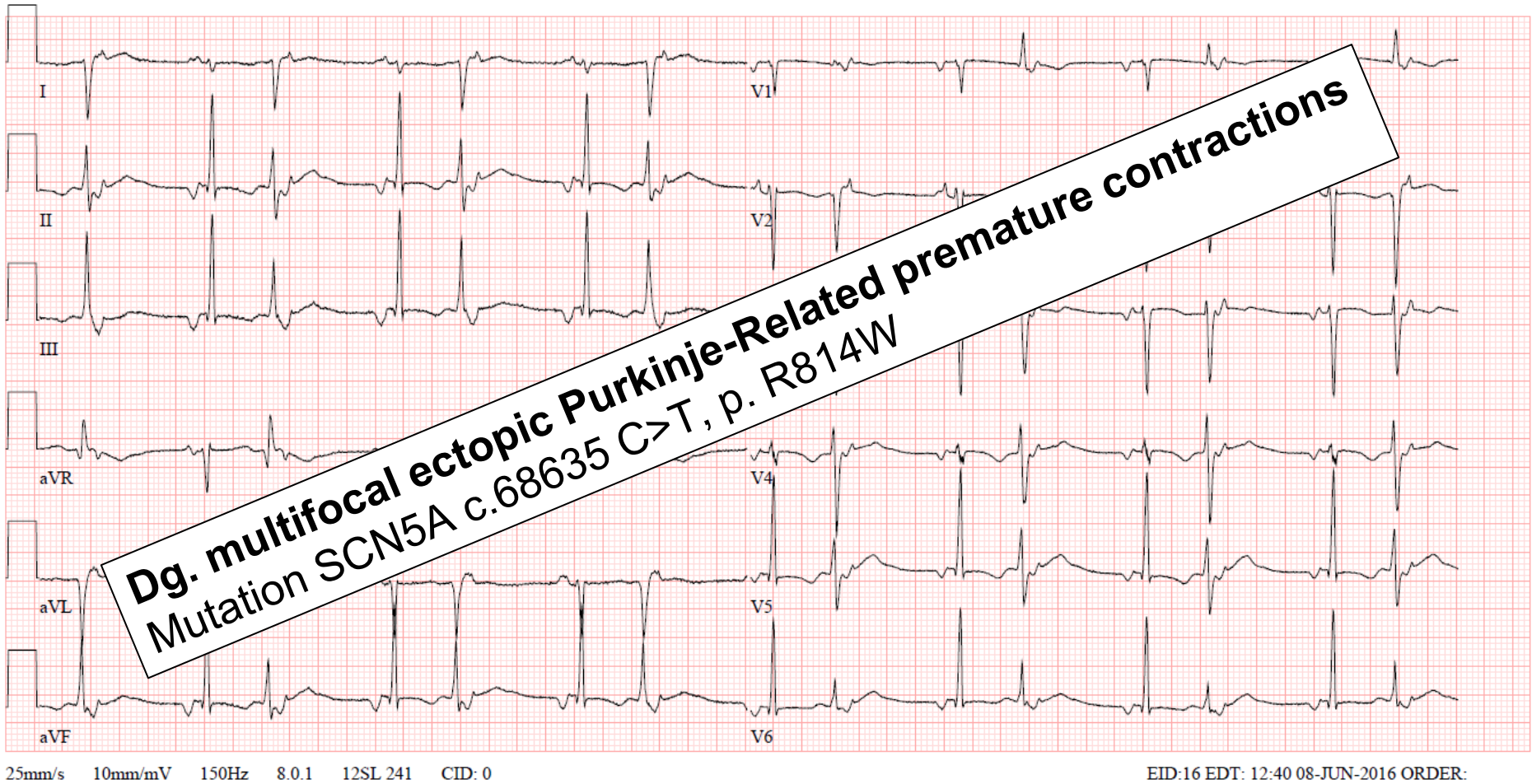
# A case of LV summit ectopy

## Alcohol ablation of coronary sinus branch



Echogenicity in the LV summit after alcohol injection

# 39-year old female with very frequent „narrow“ PVCs nad low LV EF 25%

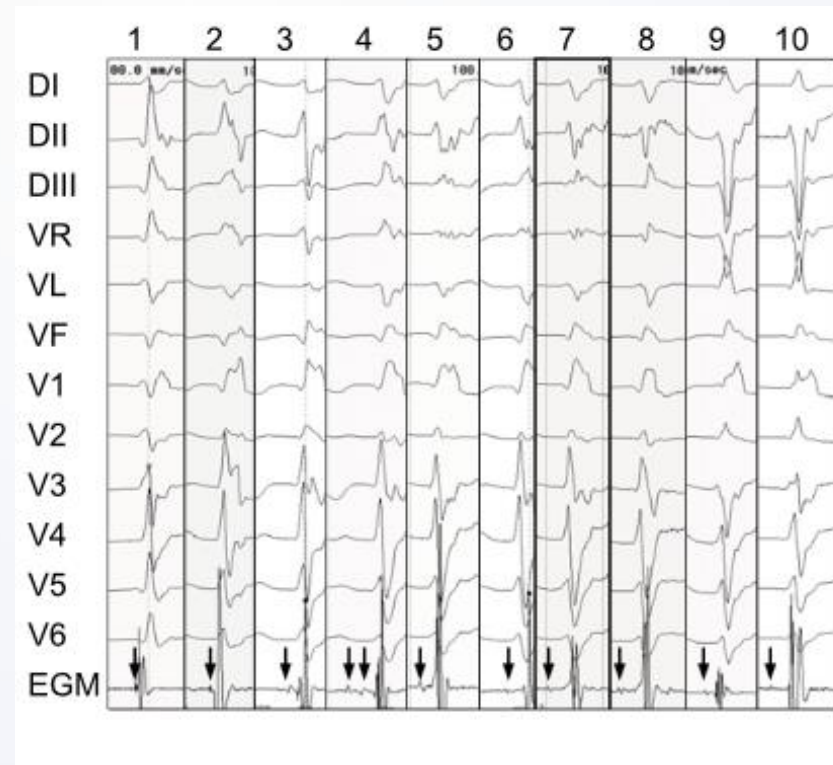




# MMEPC

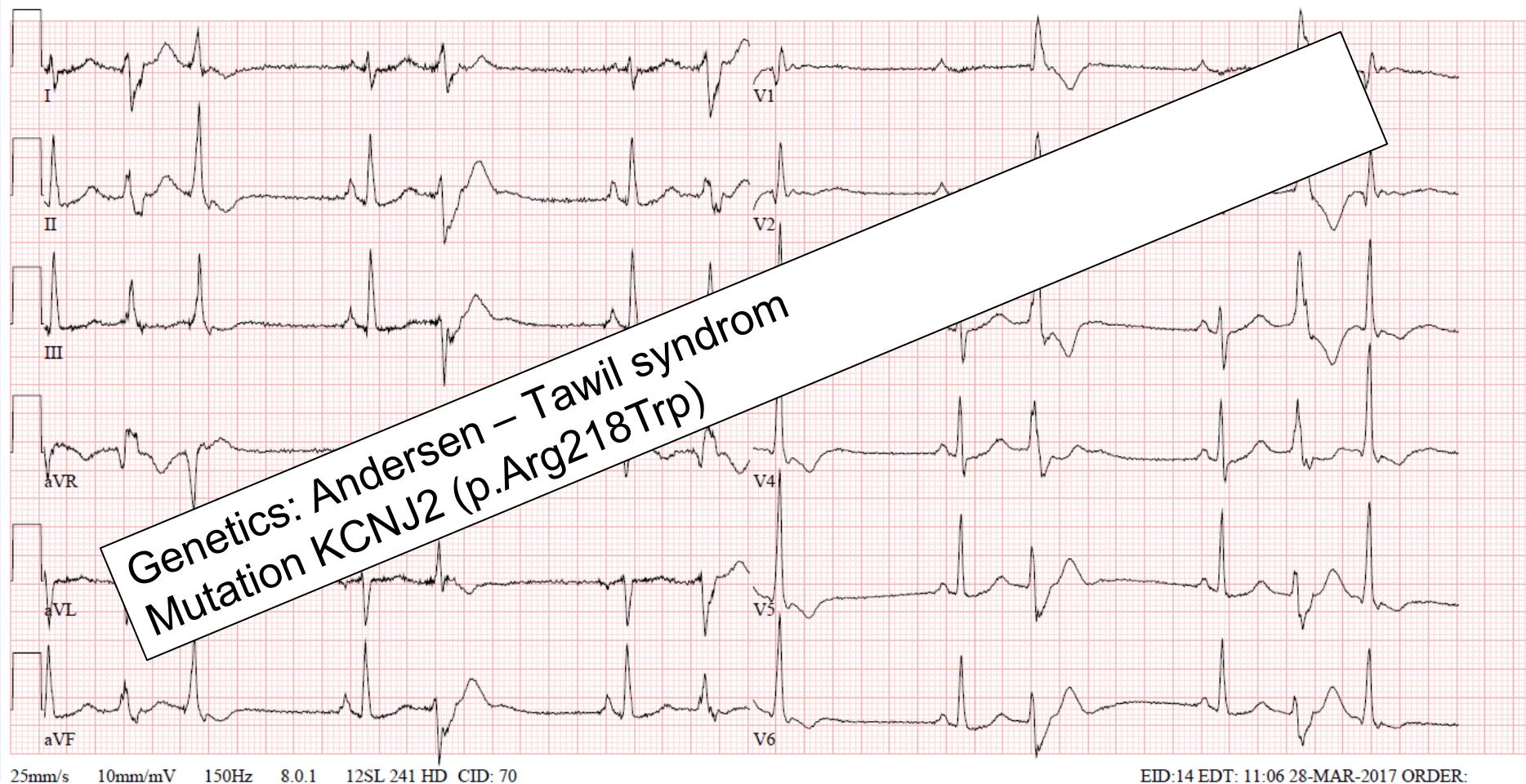
## Multifocal ectopic Purkinje-related premature contractions

- Mutation in SCN5A gene leading to the abnormal repolarization of Na channel
- Typical ECG pattern of junctional and very frequent PVBs originating from conduction system associated with LV dysfunction and sudden cardiac death
- Therapy: hydroquinidine





# 41-year old female with very frequent symptomatic PVCs, three ablation attempts on the papillary muscles



# Tawil – Andersen syndrom

## LQT 7

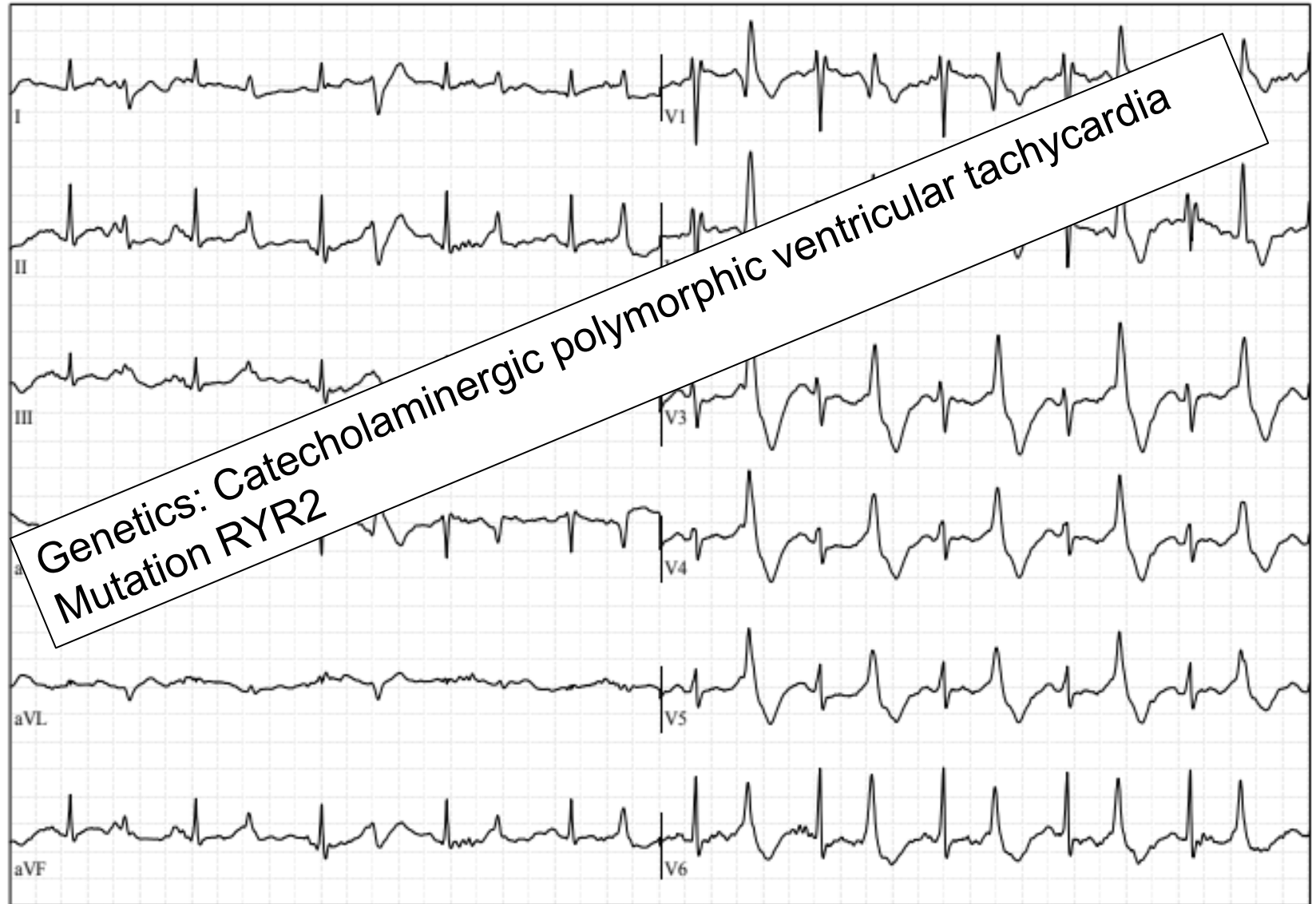
- Mutation of KCNJ2
  - Ventricular ectopy, prolonged QT with prominent U wave
  - Low-set ears, small lower jaw (micrognathia), hypertelorism, syndactily, clinodactyly
  - hypokalaemic periodic paralysis
- Treatment:
  - BB, flecainide, ICD



Fig. 1 : Showing low set ears, micrognathia and retrognathia

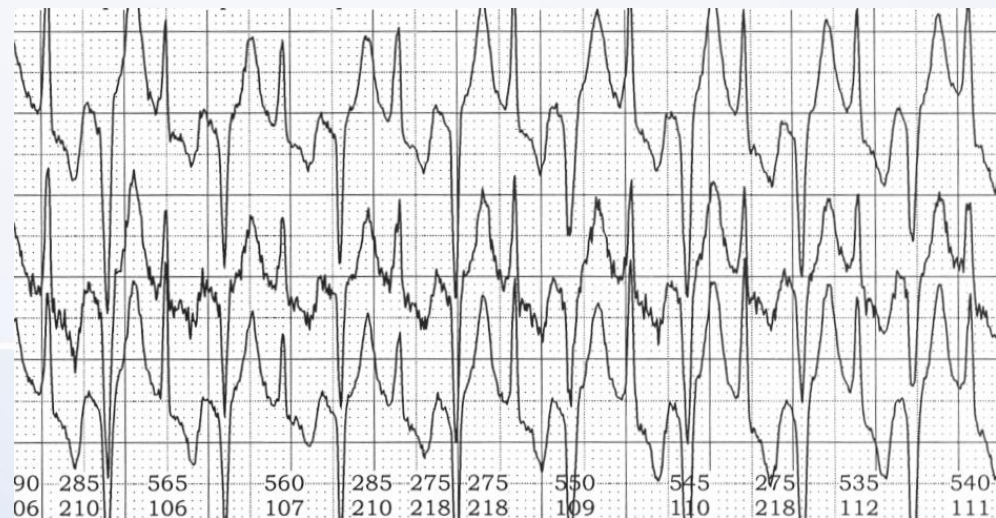
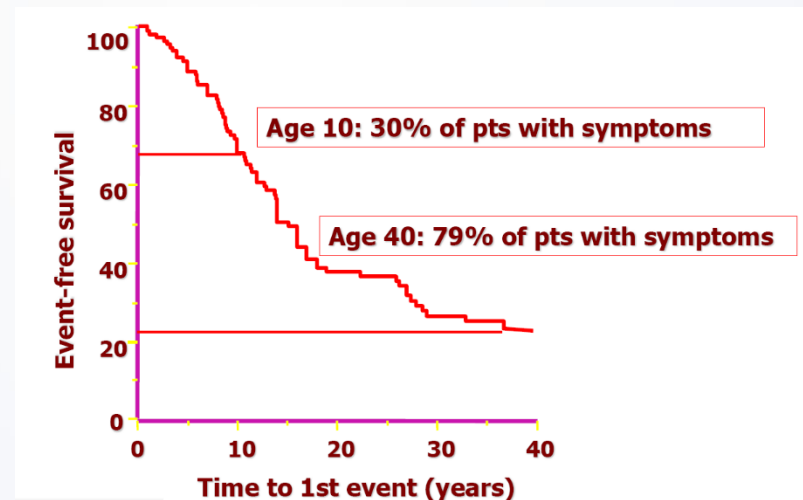


# 35year old female with PVCs during treadmill



# Catecholaminergic polymorphic ventricular tachycardia

- Triggered by physical or emotional stress
- **PVCs (bidirectional VT), polymorphic VT, atrial arrhythmias**
- Diagnosis: stress test, genetics
- Normal baseline ECG and ECHO



# Conclusions

- PVCs may be unrecognized cause of reversible LV dysfunction
- Pathophysiology of PVC induced CMP is complex and not completely understood
- Elimination of ectopy may result in normalization / improvement of LV EF (in CRT patients enables BiV pacing)
- Catheter ablation is more effective than drugs and should be indicated for patients at risk
- In-depth evaluation (including MR imaging + PES) may be used for identification patients at highest risk







# When PVCs may lead to CMP?

- **Frequency:**

- Threshold is not clearly defined
  - >10-20,000 PVCs/24hours, or >20% beats/24 hours,
- Baman *Heart Rhythm* 2010;7:865
  - Frequency of >24% beats has 79% sensitivity and 78% specificity for impairing LV EF

99421 QRS complexes

23796 Ventricular ectopics which represent 23 % of total QRS complexes

0 Supraventricular ectopics which represent <1 % of total QRS complexes

0 Paced QRS complexes which represent <1 % of total QRS complexes

- **PVCs origin:**

- Ectopy from RV has higher hemodynamic impact than ectopy from LV (similarly with QRS>140ms)
- Munoz *JCE* 2011;22:791
  - PVCs are significant if from RV>10,000 or from LV>20,000